REMARKS

Claims 30-32, and new claims 112-118 will be pending in the present application upon entry of this amendment. Support for new claims 112-118 is found throughout the application, e.g., at paragraphs 17 and 18. Claims 30 to 32 have been amended to expedite prosecution and support for the amendments is found throughout the specification, e.g., at paragraphs 17 and 18. Claim 32 has also been amended to recite a feature of a CatSper2 protein. Support for this amendment is found throughout the specification, e.g., at Example 7 and Example 8. The present amendment is made without prejudice with respect to future prosecution. No new matter is believed to be added by the amendment.

35 U.S.C. § 112, Enablement

Claims 29, 31, and 32 have been rejected for alleged lack of enablement. Claim 29 has been canceled and new claims 112-118 are added by the present amendment.

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (*United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988)). The Office Action states that the application is enabled "for polypeptides comprising the sequence of SEQ ID NO:2 or fragments completely contained within the sequence of SEQ ID NO:2" (Office Action at page 4, item 5). Claim 30 is drawn to polypeptides comprising the sequence of SEQ ID NO:2 (as well as SEQ ID NO:4 and SEQ ID NO:6) and to fragments contained within those sequences. New claim 112 is drawn to polypeptides consisting of such sequences. Applicants therefore submit that claims 30 and 112 are clearly enabled per the statement of the Office Action.

The Office Action also states that the application "does not reasonably provide enablement for a CatSper2 protein, fragments of a CatSper2 protein, or polypeptides 80% identical to a Catsper2 polypeptide." Applicants understand this to refer to those claims drawn to a sequence that has 80% identity to a CatSper2 protein or fragment of such a protein. To expedite prosecution, the claims have been amended such that all claims recite SEQ ID NOs for CatSper2 proteins. Therefore, comments in the Office Action regarding the definition of a CatSper2 protein (without recitation of a specific SEQ ID NO) are, only for purposes of the present application, rendered moot.

With respect to claims drawn to a polypeptide having at least 80% identity to a CatSper2 protein, Applicants assert that such a claim is amply enabled by the specification.

Claim 31 has been amended to recite a polypeptide having at least 80% identity with a CatSper2 protein having a specific amino acid sequence (SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6) or a fragment of such a protein. One in the art would readily understand how to make a protein having at least 80% identity to a recited sequence of a CatSper2 protein. Uses for such proteins are also provided in the application. For example, a mutation in a Catsper2 protein or a fragment of such a protein with such a mutation may have at least 80% identity with a wild-type protein. Such proteins can be used, for example, for generating an antibody to detect a mutant protein for diagnostic purposes (see specification at paragraph 109 and paragraph 125). Because the specification combined with what is well known in the art provides information on how to make and use a Catsper2 protein or fragment that is not identical to a wild-type CatSper2, Applicants submit that claim 31 is enabled.

Claim 32 has also been amended to recite a polypeptide having at least 80% identity with a CatSper2 protein having a specific amino acid sequence (SEQ ID NO:2, SEQ ID NO:4, of SEQ ID NO:6) and at least one feature or activity of a CatSper2 protein. Support for enablement of a protein or fragment having at least 80% identity with a CatSper2 is discussed above.

With respect to features and activities of a CatSper2 protein, the specification discloses a number of features and activities of a CatSper2 protein. For example, disclosed features of a CatSper2 protein include expression of CatSper2 in testis (e.g., Example 5 of the specification), localization of a CatSper2 protein to epididymal sperm membranes (Example 8), localization of a CatSper2 protein to sperm flagella (Example 8). The specification discloses a number of CatSper2 activities, for example, at paragraphs 118 and 120, and e.g., at paragraph 37

> As used herein "CatSper2" activity means any normal biological activity of a wild-type CatSper2 protein when expressed in a cell or cell type in which CatSper2 is normally expressed and under conditions under which CatSper2 is normally expressed. Such activity can include induction of an ion current; mediation of cAMP-induced Ca^{2+} influx; restoration of sperm motility when expressed in CatSper2-/- sperm; and/or restoration of the ability to penetrate eggs when expressed in CatSper2-/- sperm. CatSper2 activity can be measured in sperm cells or spermatocytes, or in other cells in which any necessary accessory factors are present.

The Office Action focuses only on a single activity of a CatSper2 protein - ion channel activity, and appears to contradict Applicants' statements that CatSper2 is not a channel protein. The Office Action presents Example 10 of the specification as evidence that the disclosed CatSper2 sequences "do not appear to act as cation channels" (Office Action at page 8). Applicants assert that Example 10 is not relevant to the whether CatSper2 protein is a channel protein and that the Office Action mischaracterizes Example 10. The results of Example 10 show "that CatSper2 alone does not form a functional ion channel in these cells." (Specification at paragraph 195). Thus, Applicants, who bear the presumption of expertise in their field, interpret the data as indicating that a CatSper2 protein functions in concert with other proteins to form a functional channel. Contrary to the statements in the Office Action, these data do not contradict the discovery of Catsper2 as a channel protein. Applicants therefore submit that any rejections presented in the Office Action asserting a lack of enablement based on this erroneous interpretation of Example 10 should be withdrawn

In furtherance of the rejection of claims drawn to a "CatSper2 protein," the Office Action states "only experimental evidence can confirm functional similarity of sequence related by a given percent identity or homology as taught by Skolnick et al. (2000, Trends Biotechnol. 18(1):34-39) and Whisstock et al. (2003, Quart. Rev. Biophys. 36:307-340) (Office Action at page 8, first full paragraph). Applicants disagree with the characterization of Skolnick et al. and Whisstock et al. as constituting rejection of sequence-based approaches to determining protein function.

Skolnick et al. states "[a]lthough sequence-based approaches to protein-function prediction have proved to be very useful, alternatives are needed to assign the biochemical function of the 30-50% of proteins whose function cannot be assigned by any current methods." (Skolnick et al. at page 37, second column, last paragraph). Applicants assert that CatSper2 is a protein whose function can be assigned by current methods, and Applicants have done so, as evidenced by the present application. Furthermore, the identification of CatSper2 as a channel protein does not rely solely on sequence analysis, but also on an analysis of motifs and domains, and expression, and localization data (e.g., Fig. 1, Examples 3-5, 7, 8, and 10. Whisstock et al. Office Action further indicates "if there is a standard method of predicting protein function, it is the detection of similarity of amino-acid sequence by database searching, and assuming that the molecules identified are homologues with similar functions." Thus, both of these references

indicate that it is common and even "standard" practice among those in the art to use sequence analysis for identification of proteins with similar functions. As discussed above, Applicants did not merely use sequence similarity to identify function for CatSper2, but also for motif and domain analysis, expression, and localization data. Applicants therefore submit that the citations of Skolnick et al. and Whisstock et al are irrelevant to the claimed invention, both because they do not constitute complete rejections of the use of sequence analysis to characterize a protein, and because sequence analysis was not the sole method used to characterize CatSper2. Accordingly, Applicants submit that the Office Action is incorrect in asserting that CatSper2 is not a cation channel and that any rejection based on that assertion should be withdrawn.

The Office Action also states "The specification does not appear to disclose a utility for antibodies that cannot bind the wild-type CatSper2 sequences of SEQ ID NOs:2, 4, or 6, and as such the polypeptides that can be used to generate said antibodies do not appear to be enabled. Applicants respectfully disagree. The specification states "[p]oint mutations [of a CatSper2 protein], however, can also cause infertility and can be detected by antibodies which are specific for epitopes including or affected by the mutant species." (Office Action at paragraph 109). Proteins that are not identical to a wild-type CatSper2 protein are therefore useful for generating such antibodies. Thus, contrary to the Office Action, polypeptides that are "of less than 100% identity" (Office Action at page 8, first full paragraph) to a CatSper2 (such as those having at least 80% identity to a CatSper2 protein) do, in fact, have a disclosed use and Applicants submit that such polypeptides are enabled by the specification.

In view of the above arguments, Applicants believe that the pending claims are fully enabled and respectfully request that the 35 U.S.C. § 112, enablement rejection be withdrawn.

35 U.S.C. § 112, Written Description

Claims 29, 30, and 32 have been rejected for alleged lack of written description. Claim 29 has been canceled. With respect to written description, the Federal Circuit has established that "[t]he applicant must ...convey to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563-64 (Fed Cir. 1991). The Office Action states "Applicant is in possession of the proteins of SEQ ID NOs: 2, 4, and 6." (Office Action at page 9, second paragraph). However, the Office Action also states that Applicants are "not in possession of the genus of all CatSper2 proteins, proteins 80%

identical to a CatSper2 protein, or proteins comprising fragments 80% identical to a CatSper2 protein." (Office Action at page 9, third paragraph). To expedite prosecution of the present application, claims drawn to CatSper2 proteins have been canceled or amended to recite specific CatSper2 sequences (i.e., SEQ ID NO:2, SEQ ID NO:4, and SEQ ID NO:6).

Regarding claims drawn to polypeptides that are at least 80% identical to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6 and fragments of such sequences, Applicants submit that one in the art would recognize that Applicants were in possession of the claimed sequences since one in the art would readily know how to identify a sequence having at least 80% identity to SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6, or fragments thereof. Applicants also submit that ample written description of the function of CatSper2 protein sequences, their motifs, domains, features, and activities are provided in the specification. This includes, as described above reference to, e.g., point mutations in a Catsper2 protein, and uses related to such proteins (e.g., paragraph 109 of the specification). Thus, Applicants submit that the specification provides functional characteristics of CatSper2 proteins, known/disclosed correlations between structure and function, structural features including sequence and identification of domains and motifs.

The Office Action appears to base the written description rejection largely on a misinterpretation of Example 10, which, as discussed above, and contrary to the assertions of the Office Action, does not demonstrate that CatSper2 lacks channel activity, but merely demonstrates "that CatSper2 alone does not form a functional ion channel in these cells." (Specification at paragraph 195). The assertions of the Office Action regarding the identity of CatSper2 proteins as channel proteins are thus in error and should be withdrawn.

In view of the arguments presented above, applicants submit that that the claims meet the written description requirement under 35 U.S.C. § 112, and respectfully request that the rejection under 35 U.S.C. § 112, written description, be withdrawn.

35 U.S.C. § 102 (b)

Claims 29-32 are rejected as allegedly anticipated by Rosen et al. (WO 00/61624 A1). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The Examiner states that Rosen et al. "teach a polypeptide that is 100% identical to amino acids 108-350 of

SEQ ID NO:2." (Office Action at page 12, second paragraph). The Rosen et al. sequence is 243 amino acids in length and, at a minimum, lacks the N-terminal, C-terminal, and transmembrane segment 1 of a Catsper2 protein.

None of pending claims 30-32 or 112-115 are drawn to sequences contained entirely within the Rosen et al. sequence. Therefore the Rosen et al. sequence does not contain every element of any of the pending claims and Rosen et al. cannot anticipate the claims.

In addition, Rosen et al does not appear to provide any information identifying functional domains of the Rosen et al. sequence. Since Rosen et al. did not disclose any functional domains, the reference does not anticipate new claims 116, 117, or 118, which are drawn to include specific functional domains.

In view of the amendments to the application and the discussion above, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b).

CONCLUSION

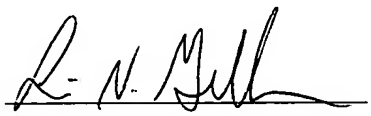
It is believed that all of the pending claims have been addressed. However, the absence of a reply to a specific rejection, issue or comment does not signify agreement with or concession of that rejection, issue or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

In view of the above amendment and remarks, applicants believe the pending application is in condition for allowance, which action is respectfully requested

This Amendment in Response to Final Office Action is being filed with a Petition for Extension of Time. Please charge any payments due or credit any overpayments to our Deposit Account No. 08-0219.

Respectfully submitted,

Dated: 18 August 2006



Lisa N. Geller
Registration No.: 51,726
Attorney for Applicant(s)

Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, Massachusetts 02109
(617) 526-6000 (telephone)
(617) 526-5000 (facsimile)